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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,930	03/22/2001	Ellen Heber-Katz	00486.00006	1820

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EXAMINER
LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
1635	11

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/813,930	HEBER-KATZ, ELLEN	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,15-22,24 and 25* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,15-22,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restriction

Claims 3-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 15-22, 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "low normal level" in claim 1 is a relative term which renders the claim indefinite. The term "low normal level" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification provides a range of normal levels of T3 and T4 for mice (see page 10) and the prior art provides normal ranges for thyroid hormone levels for other species, however, within those ranges it is unclear what would be considered "low" normal, rather than, for example, high or mid normal. The specification does not define the range within normal for "low normal", nor does the prior art have a set level within the

normal range that would be considered "low normal". Claims 2, 15-22, 24 and 25 are rejected for the same reasons due to dependence on claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 15-22, 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

In the amendments filed April 27, 2003, claim 1 has been amended to include the limitation wherein the amount of thyroid hormone-lowering agent administered in the claimed methods is "effective to decrease a level of a thyroid hormone in the mammal to a low normal level or to a below normal level". Support for this limitation could not be found in the originally filed claims or specification and, therefore, is considered to be new matter. Applicant points to Example 5 in the specification to support the newly added limitation, as Example 5 teaches low normal and below normal levels of thyroid hormones in healer versus non-healer mice. Example 5, however, does not support the new limitation "effective to decrease a level of a thyroid hormone in the mammal to a low normal level or to a below normal level" in the claimed methods because example 5

presents the level of two hormones (T3 and T4) as an observed phenotype for a strain of mice. Although the T3 and T4 levels measured in this strain of mice may fall within the scope of low normal or below normal, these levels were not as a result of administration of a thyroid hormone lowering agent, but are the natural levels for this strain of mice. Further, there is no indication in claim 5, or anywhere else in the specification, that lowering thyroid hormones to the level observed in the healer mice is contemplated as a method of the invention, or that the range of low normal or below normal is a particular range contemplated by the inventor. Nor is there any indication in Example 5, or anywhere else in the specification, that the methods of the invention are practiced by administering an amount of an agent that lowers the level of a thyroid hormone to low normal or below normal levels. Therefore, the limitation "effective to decrease a level of a thyroid hormone in the mammal to a low normal level or to a below normal level" is considered to be new matter. Claims 2, 15-22, 24 and 25 are dependent upon claim 1 and, therefore, also directed to encompass the new matter and are rejected for the same reasons.

Response to Amendments

The rejection of record of claims 1, 2, 16-19, 21 and 23 under 35 U.S.C. 102(b) as being anticipated by Corte et al. (Gazz Med Ital Arch Aci Med, 1993, 152:149-153), set forth in the prior Office action mailed January 22, 2003, is withdrawn in response to Applicant's amendments filed April 7, 2003. Corte et al. disclose that the levels of

thyroid hormones T3 and T4 in the patient after treatment with PTU were at the highest value in the normal range, as per Applicant's Exhibit A submitted with the amendment filed April 7, 2003. Although TSH remained below normal levels in the patient of Corte et al., TSH levels were increased by treatment with propylthiouracil, relative to levels prior to treatment with propylthiouracil, and, therefore, Corte et al. do not meet all the limitations of the claimed method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 17-20, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Chappel et al. (Endocrinology, 1959, 65, p 208-215).

Chappel et al. disclose methods wherein rats were treated with propylthiouracil, and then subsequently cardiac lesions were induced in the rats using isoproterenol. Propylthiouracil administration was continued after induction of lesions and the rats treated with propylthiouracil were observed to have diminished heart lesions relative to control rats which were not treated with propylthiouracil. Chappel et al. disclose that isoproterenol induces infarct-like necrosis due to ischemia (see for example, abstract). Chappel et al. disclose that the rats were hypothyroid after treatment with

propylthiouracil, which would indicate that thyroid hormone levels were below normal. Chappel et al. do not explicitly state that re-epithelialization occurs or that T3 and T4 levels are lowered, these activities are all actions inherent to treatment with propylthiouracil (as, for example, disclosed in the instant specification) and, therefore, would be inherent to the claimed methods. Chappel et al. disclose their methods wherein they detect increased healing of the isoproterenol induced lesions. Therefore, Chappel et al. anticipate claims 1, 2, 17-20, 24 and 25.

Claims 1, 2, 16-19, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Treadwell et al. (Obstetrics and Gynecology, May 1996, 87, 5 pt 2, pages 838-840).

Treadwell et al. disclose a method wherein a human fetus is treated by oral maternal administration of propylthiouracil, effective to lower levels of T3 and T4 in the fetus to below normal levels (see for example Table 1). The fetus presented with pericardial effusion prior to treatment, which would cause damage to the pericardium, and falls within the scope of a "heart wound". This damage would be expected to continue while the effusion persisted, including damage that would occur concomitant to administration of propylthiouracil, prior to reduction of the effusion. Treatment resulted in the resolution of fetal hydrops, which would include the pericardial effusion. Treadwell et al. do not explicitly state that propylthiouracil heals damage to the pericardium of the heart or that re-epithelialization occurs, however, propylthiouracil induces healing and re-epithialization and, therefore, this activity would be expected to be inherent to the

methods disclosed by Treadwell et al., given that the methods of Treadwell et al. comprise all of the method steps of the claimed methods. Therefore, Treadwell et al. anticipate claims 1, 2, 16-19, 21 and 22.

Response to Arguments

The rejection of record of claims 1, 2, 17-20, 22 and 23 under 35 U.S.C. 102(b) as being anticipated by Alpert et al. (European Heart Journal (1984) 5 (supplement F) 3-11) are withdrawn in response to Applicant's arguments filed April 27, 2003. A closer reading of Alpert et al. indicates that the myofibrils were prepared from the left ventricle following removal of the papillary or trabecular muscle, which would require or result in the sacrifice of the rats and, therefore, healing would not occur.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523. The examiner can normally be reached on Monday-Thursday 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
June 15, 2003

Karen A Lacourciere
KAREN LACOURCIERE
PATENT EXAMINER